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Lithium and suicide prevention

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Over 800 000 people die due to suicide every year, which is the second leading cause of death worldwide (behind road traffic injuries) in 15-29-year-olds. For each adult who dies of suicide, as many as 20 others will attempt suicide [1]. Reduction of this death toll is key challenge and a comprehensive suicide prevention strategy should involve not only the health sector but also education, employment, social welfare and others stakeholders [1]. However, mood disorders are common disorders with an elevated risk of early death from suicide and mood disorder-related suicide should be a particular focus of concern. The role of treatment (including medication) in suicide prevention is an important and often neglected topic. However, medicines which have proven good evidence for a suicide prevention effect are rare. Lithium was eventually fully accepted as a treatment for patients with psychiatric disorders some time after John Cade's initial report in 1949. After more than six decades of study, the efficacy of lithium as a treatment for mood disorders (both bipolar and unipolar), as shown in meta-analyses of clinical trials, is robust and these analyses also show clear effects of lithium in reducing suicide (both attempts and completed suicide). Cipriani et al [2] recently reported that compared to placebo, lithium treatment reduces mortality and suicide by more than 60% in patients with major depression or bipolar disorder (BD). Notably, other mood stabilizers, such as valproate and other anticonvulsants, have only weak effects on suicide compared with lithium [2]. Lithium, as well as being available as a medicine, is an element present in trace amounts to a variable degree in the environment. Multiple studies have suggested that environmental lithium concentrations are negatively associated with reduced suicide rates since the first paper was published in 1990 [3]. Clinical and epidemiological studies also suggest that the antisuicidal effects of lithium may be greater in males than females [4, 5].

Evidence from patients with other mental disorders, behavioural disturbances and emotionally unstable personality disorders suggest that the antisuicidal effect of lithium is not simply a by product of its mood stabilising properties.

Lithium's antisuicidal effect is paralleled by an anti-aggressive effect, both of which may be mediated by effects on serotonergic neurotransmission. Impulsivity and aggression have been associated with death by suicide and are among the most frequently implicated risk factors for engaging in suicide behaviour ^[6]. Higher levels of lithium in the drinking water may therefore decrease suicide rates by reducing impulsivity and aggression ^[7]. Though lithium salts have adverse effects, especially to kidney and thyroid function, these can be mitigated by careful monitoring ^[8]. One further problem with lithium treatment is that abrupt discontinuation is associated with increased mania and suicidal behaviour ^[9]. Assurance of good compliance is therefore essential. Improvement of clinical practice might be facilitated by education of both clinicians and patients about lithium's benefits and harms. Improved monitoring reduces adverse long-term effects, and education about lithium is included in psychoeducational treatment strategies ^[10].

The association of increased levels of environmental lithium with reduced rates of completed suicide raises the hypothesis that a prescription at low or very low doses of lithium may provide well-tolerated, effective prevention of suicide in populations with high suicide risk, including patients with mood disorders. Potentially, psychiatrists may separate the mood stabilization effect and antisuicidal effect of lithium treatment as different dosages are needed. However, the clinical trials which would be required to verify the benefits of this approach would be expensive, challenging and would require a major investment in research in this area.

Suicide is a major public health problem worldwide and lithium is one of the few interventions which have been shown convincingly to reduce suicide rates when used to treat mood disorders. This is very important and strengthens the case for using lithium in appropriate clinical populations. The recent findings that greater environmental lithium levels reduce suicide rates at a population level are intriguing. Future research should focus on understanding the neural mechanism of this effect and whether this phenomenon may inform future public health strategies.

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